

10/15/19 19:43

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date
31 December 2003 (31.12.2003)

PCT

(10) International Publication Number
WO 2004/000236 A3

(51) International Patent Classification⁷: C12N 15/00, 1/21, 15/11, C07H 21/04, C07K 14/00

(21) International Application Number: PCT/US2003/020111

(22) International Filing Date: 25 June 2003 (25.06.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data: 60/391,285 25 June 2002 (25.06.2002) US

(71) Applicant (for all designated States except US): THE OHIO STATE UNIVERSITY RESEARCH FOUNDATION [US/US]; 1960 Kenny Road, Columbus, OH 43210 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): JHIANG, Sissy, M. [US/US]; 1492 Markland Street, Columbus, OH 43235 (US). SHEN, Daniel, Hy [—/US]; 2540 Lorain Ct., Columbus, OH 43210 (US). LIN, Xiaoqin [CN/US]; 581 Harley Dr. #6, Columbus, OH 43202 (US).

(74) Agent: DOCHERTY, Pamela, A.; Calfee, Halter & Griswold LLP, 800 Superior Avenue, Suite 1400, Cleveland, OH 44114 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv)) for US only

Published:

— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report: 8 July 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MODIFIED SODIUM IODIDE SYMPORTER PROTEINS AND GENES FOR IMAGING AND CANCER THERAPY

(57) Abstract: The invention provides modified sodium iodide symporter (NIS) proteins, and polynucleotides encoding modified NIS proteins. The modified NIS proteins have a net electrostatic charge more positive than that of corresponding wild-type NIS proteins. Expression of a modified NIS protein in a cell results in higher intracellular concentrations of NIS substrates as compared to equivalent expression of the corresponding wild-type NIS protein in a cell. The invention also provides methods for imaging cells or for therapy of cancer cells, using the modified NIS proteins to facilitate transport of NIS substrates into cells in the body of an individual. Uptake of NIS substrates suitable for either imaging or that have cytotoxic activity, into the cells of the individual that express modified NIS protein facilitate detection of the substrate (for imaging) or killing of the cancer cells (for therapy).

WO 2004/000236 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/20111

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 15/00, 1/21, 15/11; C07H 21/04; C07K 14/00
 US CL : 435/69.1, 252.3; 536/23.1, 23.5; 530/350

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/69.1, 252.3; 536/23.1, 23.5; 530/350

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6,391,579 B1 (CARRASCO et al) 21 May 2002 (21.05.2002), see columns 4-9.	25-33
---		-----
Y		1-24
Y	HUANG, M. et al. Ectopic expression of the thyroperoxidase gene augments radioiodide uptake and retention mediated by the sodium iodide symporter in non-small cell lung cancer. 2001, Vol. 8, No. 8, pages 612-618, especially page 612 and 617, left column.	1-24, 29-32
Y	JHIANG, S. M. Regulation of Sodium/Iodide Symporter. Reviews in Endocrine and Metabolic Disorders. 2000, Vol. 1, pages 205-212, see especially page 205, right column and pages 213-214.	1-24, 29-32
Y	SHEN, D. H. Y. et al. Sodium Iodide Symporter in Health and Disease. Thyroid. May 2001, Vol. 11, No. 5, pages 415-425, see entire document.	1-33

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier application or patent published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

01 May 2004 (01.05.2004)

Date of mailing of the international search report

21 MAY 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
 Commissioner for Patents
 P.O. Box 1450
 Alexandria, Virginia 22313-1450

Faxsimile No. (703)305-3230

Authorized officer

David J Blanchard

Telephone No. (571) 272-1600

J. Roberts for

Continuation of B. FIELDS SEARCHED Item 3:

Medline, Biosis, EMBASE, Cancerlit, Biotechno CAPLUS, WEST.

Search terms: NIS, symporter, , radioiodide, iodide retention, iodination, modified and mutant NIS, inventor search